

inactivation by means of a transposon inserted into the gene, so that it is defective in spread within infected cells and from infected to uninfected cells of the host.

25. The method of claim 24, further comprising inactivating an aerobactin or enterochelin gene of the wild strain of *Shigella*, other than only by inactivation by means of a transposon inserted into the gene, so that it is defective in invading cells of a host.

26. The method of claim 25, further comprising inactivating a *Shiga*-toxin gene of the wild strain of *Shigella*, other than only by inactivation by means of a transposon inserted into the gene, so that it is defective in killing host cells.

27. The method of any of claims 24-26, wherein said *Shigella* is *S. flexneri*.

28. The method of any of claims 24-26, wherein said *Shigella* is *S. dysenteriae* 1.

29. The method of claim 28, wherein one or more of the ent F, Fep E, Fep C, and Fep D subunit genes of the enterochelin operon of *S. dysenteriae* 1 are modified.

30. The method of claim 26, wherein the *Shiga*-toxin gene is the *Shiga*-toxin A gene.

31. The method of any of claims 24-26, wherein one or more of said genes are inactivated by allelic exchange with one or more mutagenized genes that have been mutagenized *in vitro*.

*Suk K1* 32. The method of claim 31, wherein said mutagenized genes are mutagenized genes from which nucleotide sequences have been deleted.

33. The method of claim 31, wherein said mutagenized genes are mutagenized genes into which nucleotide sequences have been inserted.

34. The method of claim 33, wherein a marker gene is inserted into said mutagenized genes.

35. The method of claim 24, further comprising isolating said modified strain of *Shigella* from said wild strain of *Shigella*.

36. A *Shigella* comprising:

- (a) an inactivated *icsA* gene, inactivated other than only by means of a transposon inserted into the gene; and
- (b) an inactivated aerobactin or enterochelin gene, inactivated other than only by means of a transposon inserted into the gene.

37. The *Shigella* of claim 36, further comprising an inactivated *Shiga*-toxin gene, inactivated other than only by means of a transposon inserted into the gene.

38. A *Shigella* comprising an inactivated *Shiga*-toxin gene, inactivated other than only by means of a transposon inserted into the gene.

39. The *Shigella* of claim 37 or 38, wherein the *Shiga*-toxin gene is *Shiga*-toxin A.

40. The *Shigella* of any of claims 36-38, wherein said *Shigella* is *S. dysenteriae* or *S. flexneri*.

41. The *Shigella* of claim 37 or 38 comprising an inactivated ent F, Fep E, Fep C, or Fep D subunit genes of the enterochelin operon.

42. The *Shigella* of any of claims 36-38, wherein one or more of said genes are inactivated by allelic exchange with ~~one or more~~ mutagenized genes that have been mutagenized *in vitro*.

*Sub A* 43. The *Shigella* of claim 42, wherein said mutagenized genes are mutagenized genes from which nucleotide sequences have been deleted.

44. The *Shigella* of claim 42, wherein said mutagenized genes are mutagenized genes into which nucleotide sequences have been inserted.

*J, conc'd* 45. The *Shigella* of claim 44, wherein a marker gene is inserted into said mutagenized genes.

46. A vaccine comprising the *Shigella* of claim 36 or 37 and a pharmaceutically acceptable vehicle. *vv*

REMARKS

Reconsideration of this application is respectfully requested.

Applicants have canceled claims 1-8, 10, and 13-23, and submitted new claims 24-46.

New claims 24-46 find support throughout the specification. No new matter enters by amendment.

Claims 1-8, 10, and 13-24 were rejected under 35 U.S.C. § 112, first paragraph.

Applicants assume that the statutory basis for this rejection is for allegedly failing to adequately teach one skilled in the art how to make and/or use the claimed invention.